46. (New) The method according to Claim 44, wherein said fluid is heated prior to said actuation.

47. (New) The method according to Claim 44, wherein an energy pulse of between about 1.0 to 100 μJ is supplied to said thermal inkjet head to expel the quantity of fluid.

48. (New) The method according to Claim 44, wherein said quantity ranges from about 0.1 to 2000 pico liters. --

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 22-24 and 27, 28 and 31-48, the only claims pending in this application.

Claims 26, 29 and 30 have been cancelled. Claims 22, 27, 31 and 34 have been amended to recite that the claimed binding agents are nucleic acid binding agents. Claim 34 has been further amended to clarify that the at least one nucleic acid binding agent that is associated with the array surface hybridizes to nucleic acid in the fluid sample. Support for these amendments may be found in the specification, e.g., at page 5, lines 5-9.

Claims 44-48 have been added. Support for these claims can be found in the specification, e.g., at page 8, line 22 through page 9, line 2; page 9, lines 12-23; page 10, lines 3-5.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version With Markings to Show Changes Made"**.

As no new matter has been added by the above amendments, entry of the above amendments is respectfully requested.

DOUBLE PATENTING REJECTION

Claims 22 and 27 were rejected under the under 35 U.S.C. §101 as claiming the same invention as that of Claims 1 and 7 of U.S. Patent No. 6,458,583 ('583). However, the Applicants respectfully submit that Claims 22 and 27 do not claim the same invention as Claims 1 and 7 of the '583 patent.

The M.P.E.P. provides guidance in this regard and states that in making rejections under 35 U.S.C. §101, a relevant question to be asked is "Is there an embodiment of the invention that falls within the scope of one claim, but not the other? If there is such an embodiment, then identical subject matter is not defined by both claims and statutory double patenting would not exist." (M.P.E.P. § 804)

The Applicants respectfully submit that there is an embodiment that falls within the scope of Claims 22 and 27 of the instant application that does not fall within the scope of Claims 1 and 7 of the '583 patent and thus a rejection of Claims 22 and 27 under 35 U.S.C. §101 in view of Claims 1 and 7 of the '583 patent cannot be sustained. Specifically, an embodiment that is characterized by not loading the nucleic acid fluid through the orifice falls within the scope of Claims 22 and 27 of the instant application and does not fall within the scope of Claims 1 and 7 of the '583 patent. As such, because this embodiment falls within the scope of Claims 22 and 27 of the instant application and not Claims 1 and 7 of the '583 patent, identical subject matter is not defined by both Claims 1 and 7 of the '583 patent and Claims 22 and 27 of the instant application.

Accordingly, because identical subject matter is not claimed in Claims 22 and 27 of the instant application and Claims 1 and 7 of the '587 patent, a statutory double patenting rejection of Claims 22 and 27 cannot be sustained and the Applicants respectfully request that this rejection be withdrawn.

REJECTION UNDER 35 U.S.C. §103(a)

Claims 22, 23, 26-31, 34, 37 and 38 were rejected under 35 U.S.C. §103(a) as being unpatentable over Milton (US 6,146,833) over Deeg et al. (US 5,338,688). Claims

26, 29 and 30 have been cancelled. In regards to the remaining rejected claims, the Applicants respectfully submit that Claims 22, 23, 26-31, 34, 37 and 38 are patentable over Milton over Deeg et al.

The M.P.E.P. provides clear guidance on the requirements of a *prima facie* case of obviousness:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."
> M.P.E.P. § 2142.

Accordingly, in order to be rendered obvious by the cited references, the cited references must teach or suggest all of the claim limitations. However, the Applicants respectfully submit that the cited references either alone or when combined do not teach or suggest all of the claim limitations.

For example, the methods of Claims 22, 23, 26-31, 34, 37 and 38 are directed towards methods of **using a nucleic acid array**, i.e., the subject methods are concerned with using an array whereby fluid is deposited onto the array using a thermal inkjet head. More specifically, as amended, independent Claims 22, 27, 31 and 34 recite that the array surface, onto which a quantity of fluid containing nucleic acid is deposited, **includes a plurality of nucleic acid binding agents stably associated with it.** The instant application makes it clear that the term "binding agent" refers to a member of a specific binding pair (see for example page 3, lines 17-19) and that "complementary nucleic acids" are an exemplary binding pair, in which one member is stably associated to a support surface (page 5, lines 7-9).

Thus, the subject methods clearly recite that the surface onto which the fluid is deposited is an array surface, specifically a previously prepared array and more specifically a surface that includes a plurality of nucleic acid binding agents stably

associated with it. Accordingly, the subject invention is concerned with using arrays in array-based analyte detection assays and specifically **hybridization** assays between nucleic acid in a fluid sample and an array or rather nucleic acid binding agents present on a surface of an array. Moreover, each of the claims also recites that nucleic acids present in the fluid sample deposited onto the array surface according to the subject methods are capable of **hybridizing to their nucleic acids complements**.

Thus, in order for the subject claims to be rendered obvious over Milton in view of Deeg et al., the references must teach or suggest the deposition of fluid containing nucleic acids onto a previously prepared array surface using a thermal inkjet head such that the deposited nucleic acids are capable of hybridizing to their nucleic acids complements.

However, the Applicants respectfully submit that the cited references do not teach or suggest these claim limitations because the references are directed towards the manufacture of arrays and not the use of the arrays, as is claimed in the subject claims.

Specifically, Milton does not teach depositing a quantity of nucleic acid containing fluid onto a substrate surface that includes a plurality of nucleic acid binding agents stably associated with it. In fact, the Examiner correctly points to specific passages in Milton for "teaching binding oligonucleotides to support activated with acyl fluoride functionalities (Office Action, page 4). As such, the Examiner acknowledges that Milton teaches a support activated with acyl fluoride functionalities – not a support having a plurality of nucleic acid binding agents as claimed in the subject claims.

Thus, Milton teaches reagents and processes for immobilizing biopolymers and biomonomers to a solid support. Generally, Milton et al. teach that these biopolymers and biomonomers are immobilized to the solid support by their interaction with acyl fluoride functionalities present on the surface of the solid support (abstract; col. 3, entirety to col. 4, lines 1-36). Specifically, Milton teaches contacting the acyl fluoride functionalized support with "...a suitably derivitized biopolymer or derivitized biomonomer under

conditions which cause the derivitized biomonomer or biopolymer to react with acyl fluoride functionalities" (col. 10, lines 1-4). Thus, Milton teaches the immobilization of a biopolymer or biomonomer to acyl fluoride groups present on a solid support. Milton also teaches "Processes for immobilizing biopolymers to activated solid support surfaces and directly attaching in a step-wise successive manner biomonomer units to a growing biopolymer chain attached to the solid support." (abstract) Accordingly, nowhere does Milton describe that a thermal inkjet head is utilized to contact a fluid sample with a previously prepared array, i.e., a support having nucleic acid binding agents associated with it.

Furthermore, Milton does not even suggest a substrate surface having a plurality of nucleic acid binding agents thereon as Milton is concerned with forming and synthesizing immobilized biopolymers on a substrate surface, i.e., manufacturing or making an array, and not with performing hybridization assays using an already prepared array, wherein a fluid containing nucleic acid is contacted with its complementary nucleic aid binding agent present on an array surface to form a binding complex made up of the complementary binding pair. As such, there is no need for the solid support of Milton to have a plurality of nucleic acid binding agents thereon, as claimed in the subject claims, because Milton is concerned with making an array and not concerned with complementary binding pairs and more specifically is not concerned with hybridization reactions between nucleic acid binding agents on a substrate surface.

Deeg et al. is cited solely for actuating a thermal inkjet head and thus Deeg et al. fail to make up for the deficiencies of Milton et al. In fact, Deeg et al. is not even concerned with utilizing a thermal inkjet to deposit a fluid containing a nucleic acid nor is Deeg et al. concerned with an array substrate having a plurality of nucleic acid binding agents stably associated therewith as Deeg et al. is only concerned with deposition of protein agents, e.g., enzymes and antibodies. Accordingly, Deeg et al. does not teach or suggest the use of the disclosed device in conjunction with nucleic acid molecules and in fact nowhere in Deeg et al. is the term "nucleic acid" even employed.

Specifically, analogous to Milton et al. Deeg et al. is directed towards using a jet from a jet unit to **manufacture or make** reagent domains (32) on a band (20) (see for example col. 4, lines 37-46) and not to deposit a fluid sample using a jet unit onto a support that already has nucleic acid binding agents thereon as claimed in the subject claims. While Deeg et al. do teach that a sample may be delivered downstream from the jet units of Deeg et al. by sample metering unit (28) to the reagent domains (32), nowhere is it taught that these sample metering units are jet units and in fact FIG. 2 of Deeg et al. clearly shows these metering units as different from the jet units shown. Likewise, while Deeg et al. do teach that additional reagent metering station (31) enables a further reagent to be metered, as noted above nowhere is it taught or even suggested that this metering station deposits a nucleic acid, let alone nucleic acids that are capable of hybridizing to their nucleic acid complements, where such is claimed in the subject claims.

Accordingly, because the cited references fail to teach or suggest all the claim limitations, a proper *prima facie* case of obviousness under 35 U.S.C. §103(a) cannot be made and the Applicants respectfully request that this rejection be withdrawn.

Claims 24, 32, 33, 35, 36 and 39-43 were rejected under 35 U.S.C. §103(a) as being unpatentable over Milton (US 6,146,833) over Deeg et al. (US 5,338,688) in further view of Cornell (US 6,132,030). The Applicants respectfully submit that Claims 22, 23, 26-31, 34, 37 and 38 are not unpatentable over Milton and Deeg et al.

As described above, Milton and Deeg et al. do not teach utilizing a thermal inkjet head for the deposition of a quantity of nucleic acid containing fluid onto a substrate surface that has a plurality of nucleic acid binding agents stably associated with it. As Cornell is cited solely for teaching the use of specific power requirements in determining the heat power density for ejecting from thermal inkjet, Cornell fails to make up for the deficiencies of Milton and Deeg et al. Accordingly, for reasons analogous to those described above, the Applicants respectfully submit that a proper *prima facie* case of obviousness cannot be made and thus request that this rejection be withdrawn.

CONCLUSION

The applicant respectfully submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Gordon Stewart at 650 485 2386. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,

Date: 2.3.03

By: _____
Bret E. Field
Registration No. 37,620

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

22. (Amended) A method for depositing a quantity of fluid containing a nucleic acid~~, on~~ onto an array ~~substrate~~ surface having a plurality of nucleic acid binding agents stably associated therewith, said method comprising:

positioning a thermal inkjet head filled with said nucleic acid containing fluid in opposing relation to said substrate surface; and

actuating said thermal inkjet head in a manner sufficient to expel said quantity of fluid onto said substrate surface to deposit said quantity of fluid on said substrate surface, wherein nucleic acids present in said deposited fluid are capable of hybridizing to their nucleic acid complement.

Cancel Claim 26.

27. (Amended) A method for depositing a quantity of fluid containing a nucleic acid ~~or polypeptide~~ onto an array surface having a plurality of nucleic acid binding agents stably associated therewith, said method comprising:

loading said fluid into a thermal inkjet head comprising an orifice and a firing chamber by contacting said orifice with said fluid in a manner sufficient for said fluid composition to flow through said orifice into said firing chamber;

positioning said thermal inkjet head filled with said fluid in opposing relation to said array surface; and

actuating said thermal inkjet head in a manner sufficient to expel said quantity of fluid onto said array surface to deposit said quantity of fluid on said ~~substrate~~ array surface, wherein nucleic acids present in said deposited fluid are capable of hybridizing to their nucleic acid complement.

Cancel Claim 29.

Cancel Claim 30.

31. (Amended) A method for introducing a nucleic acid fluid sample to a nucleic acid binding agent, said method comprising:

positioning a thermal inkjet head filled with said nucleic acid fluid sample in opposing relation to a surface of an array, wherein said array comprises a plurality of nucleic acid binding agents stably associated with said surface;

actuating said thermal inkjet head in a manner sufficient to expel a quantity of said fluid sample onto said array surface wherein nucleic acids present in said deposited fluid are capable of hybridizing to their nucleic acid complement; and

allowing interaction between said fluid sample and said nucleic acid binding agent.

34. (Amended) A method for detecting the presence of a nucleic acid in a fluid sample containing said nucleic acid, said method comprising:

positioning a thermal inkjet head filled with said fluid sample in opposing relation to a surface of an array, wherein said array comprises a plurality of nucleic acid binding agents stably associated with said surface and at least one of said nucleic acid binding agents specifically hybridizes to said nucleic acid in said fluid sample;

actuating said thermal inkjet head in a manner sufficient to expel a quantity of said fluid sample onto said array surface wherein nucleic acid present in said deposited fluid are capable of hybridizing to their nucleic acid complement; and

detecting the presence of any binding complexes on said array surface between said at least one nucleic acid binding agent and said nucleic acid in said fluid sample on said array surface;

whereby the presence of said analyte in said fluid sample is detected.

Please enter the following new claims:

-- 44. (New) A method for depositing a quantity of fluid containing a nucleic acid or

polypeptide onto an array surface having a plurality of nucleic acid or polypeptide binding agents stably associated therewith, said method comprising:

loading said fluid containing nucleic acid or polypeptide into a thermal inkjet head comprising an orifice and a firing chamber by contacting said orifice with said fluid in a manner sufficient for said fluid to flow through said orifice into said firing chamber;

positioning said thermal inkjet head filled with said nucleic acid or polypeptide containing fluid in opposing relation to said substrate surface; and

actuating said thermal inkjet head in a manner sufficient to expel a quantity of said fluid onto said substrate surface to deposit said quantity of fluid on said substrate surface.

45. (New) The method according to Claim 44, wherein said method further comprises applying back pressure to said head during said contacting step.

46. (New) The method according to Claim 44, wherein said fluid is heated prior to said actuation.

47. (New) The method according to Claim 44, wherein an energy pulse of between about 1.0 to 100 μJ is supplied to said thermal inkjet head to expel the quantity of fluid.

48. (New) The method according to Claim 44, wherein said quantity ranges from about 0.1 to 2000 pico liters. --